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Thermal Modelling of Micropulsed Diode Laser Retinal Photocoagulation

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Background and Objective: **Recent studies have sought to utilize diode laser "micropulsing" in order to preserve therapeutic efficacy of retinal photocoagulation while minimizing pain and subjacent tissue injury. A model for the transient thermal tissue response to continuous and micropulsed diode laser output is presented in order to understand the laser-tissue interactions and to generate optimum parameters for exploiting potential advantages of micropulsed application.**

Study Design/Materials and Methods: **The tissue thermal response was calculated by convolving the analytical solution to the three-dimensional, isotropic heat conduction equation with a source term corresponding to the spot size of the laser incident on the absorbing retinal pigment epithelium (RPE) and choroid layers of the ocular fundus. Thermal localization is quantitated by comparing the temperature *rise* in the RPE (T(RPE)) and deep choroid (T(Ch)). A 1-watt (average power), 200-μm diameter, 100 ms pulse (continuous or micropulsed) of 810 nm radiation was modelled to be incident on a geometric idealization of the human retina and choroid.**

Results: **A temperature gradient is rapidly established with only modest temperature augmentation between 10 and 100 ms. At 100 ms, T(RPE) and T(Ch) are 32 and 23 C, respectively, for continuous application, and 41 and 27 C for 2 ms on/off micropulsed application. For a duty factor (total laser "on" time divided by pulse length) of 50%, T(RPE)/T(Ch) is maximal for a micropulse on/off duration of 2 ms; however, the variation over micropulse durations from 200 μs to 50 ms is small. In addition, whereas end-pulse T(RPE)/T(Ch) is greater for 2 ms on/off application when compared with continuous delivery (1.53 vs. 1.39), thermal relaxation during pulse quiescence in the micropulsed mode allows for an early *increase* in deep choroidal temperature with respect to T(RPE). For ten 200 μs pulses equally separated over 100 ms (duty factor=2%), T(RPE)/T(Ch)=3.2. With more numerous, lower power micropulses, T(RPE)/T(Ch) decreases monotonically to 1.39 as the duty factor is increased to 100%.**

Conclusion: **These modelling studies provide the first quantitative predictions of thermal localization achieved with diode laser micropulsing and demonstrate that short pulse lengths and low duty factors allow for maximum thermal localization. These studies will potentiate pulse-shape optimization strategies for diode laser retinal photocoagulation applications. Lasers Surg. Med. 20:409–415, 1997.** **© 1997 Wiley-Liss, Inc.**

Key words: diode; laser; photocoagulation; retina; thermal

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INTRODUCTION

The increasing availability, low cost, portability, flexibility, ease of operation, and low maintenance requirements of near-infrared diode laser sources has fueled investigation of these devices for ophthalmic applications [1–3]. In addition, when compared with visible lasers, diode laser sources operating in the near infrared offer reduced scattering and correspondingly increased transmission through nontransparent media such as cataractous lens or subretinal hemorrhage [4–7].

Recent studies have sought to exploit laser "micropulsing" in order to maintain therapeutic efficacy while minimizing untoward effects such as pain and subjacent tissue injury [8–10]. In distinction to continuous wave laser application, micropulsed application delivers a series of short pulses within a longer duration envelope potentially altering the tissue thermal response. Thermal localization potentially minimizes unintentional tissue damage that might be associated with photoreceptor injury, nyctalopia, and reduced visual field in scatter photocoagulation and reduced central acuity and scotomata in macular laser applications. Further, micropulsed application may be less painful by limiting thermal diffusion to the sensory neurons in the deep choroid.

Initial investigations cover a broad range of temporal characteristics with pulse lengths varying from 100–3,000 μs, and duty factors (total laser "on" time divided by pulse length) varying from 5–67%. However, the choice of pulse shape has not been based on a detailed understanding of the tissue thermal response to micropulsed laser application. The transient thermal tissue response to continuous and micropulsed diode laser output was investigated in order understand the laser-tissue interactions and to generate optimum parameters for exploiting potential advantages of micropulsed application.

MODEL

Near-infrared (810 nm) radiation was modelled to be incident on a geometric idealization of the human retina and choroid (Fig. 1) as described by Vogel and Birngruber [7]. The retinal pigment epithelium (RPE) and choroid were modelled as 6 and 400 μm thick, respectively, in accordance with previous models. For the RPE, melanin is assumed to be the sole absorber. Alternately, 50% of the choroidal volume is assumed

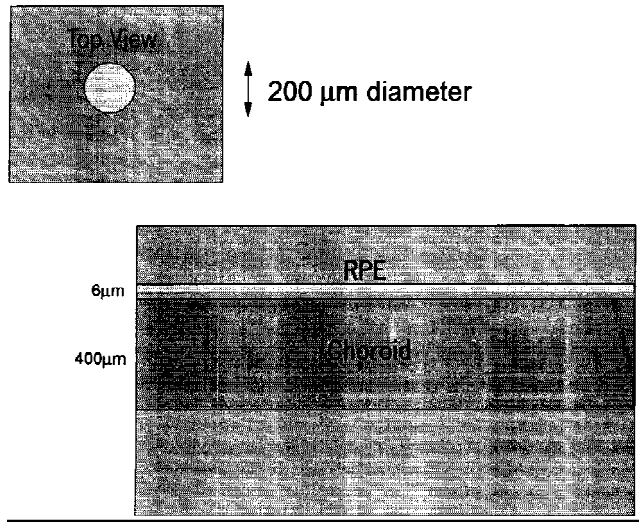

Fig. 1. Geometric idealization of the human retina and choroid. A 1 watt, 100 ms, 200 μm spot diameter, 810 nm laser pulse was modelled to be incident on a 6-μm-thick RPE with an absorption coefficient of 150/cm and on a 400-μm-thick choroid—50% blood filled—with an absorption coefficient of 7/cm. Beer's law governs the attenuation of the incident laser intensity following passage through absorbing layers of the ocular fundus.

to be filled with blood; hence both hemoglobin and melanin will absorb the near infrared light yielding absorption coefficients of 150 and 7/cm, for the RPE and choroid, respectively [7].

The tissue thermal response is calculated by convolving the analytical solution to the three-dimensional, isotropic heat conduction equation with a source term corresponding to the spot size of the laser incident on the absorbing RPE and choroid layers of the ocular fundus. Previous studies have established the insensitivity of local temperature to convective cooling associated with ocular perfusion [11]; hence a convection term is not included in the model. The temperature in a homogeneous solid is governed by the heat conduction equation,

$$\partial T/\partial t = \alpha \text{ div } (\text{grad } T) + h \qquad (1)$$

where T is a function of space and time, h is a source term reflecting heat production and transfer to the system, and α is the thermal diffusivity of the medium, where

$$\alpha = k/\rho c \qquad (2)$$

and k, ρ, and c are the thermal conductivity, density, and specific heat of the medium, respec-

tively. In general, the temperature profile in an arbitrary geometry subject to a complex source term can be solved by applying appropriate boundary conditions to the solution to equation (1). However, simplifications are required in order to allow for closed-form analytical solution or numerical integration.

A closed form expression exists for the temperature profile at a distance r and at time t following the instantaneous deposition of a heat quantity Q at time t = 0,

$$T(r,t) = (Q/((8\ \rho\ c)(\pi\ \alpha\ t)^{3/2})) \times (\exp(-r^2/4\ \alpha\ t)) \quad (3)$$

The temperature distribution is calculated by convolving this solution with a real source term extended in both space and time [11].

Analysis is limited to two dimensions by requiring cylindrical symmetry. The laser beam is modelled with a uniform, circular profile of constant fluence. The source term is defined by the solid disks corresponding to the irradiated portions of the choroid and RPE with a diameter equal to the diameter of the laser spot. Beer's law is assumed to determine the fluence of the laser light during successive transmission through the absorbing layers of the RPE and choroid.

Temperature is calculated only along the axis of symmetry, i.e., the central axis of the laser beam. Specifically, the temperature at a distance z from the inner RPE is calculated by integrating the temperature response to annuli of RPE and choroid over the laser spot size, and further integrating over the temporal profile of the laser pulse. Implicitly, a homogeneous pigment distribution in the RPE and choroid is assumed. As previously shown, thermal relaxation considerations suggest that the actual pigment distribution is of significance only for pulse durations <1 msec [11].

Temperature profiles are depicted along the central axis of the laser spot, perpendicular to the tissue planes. In these studies, a 1 watt (average power), 100 ms, 200 μm spot diameter laser pulse was modelled to be incident on the fundus geometry depicted in Figure 1. Standard values for tissue thermophysical properties are assumed: $\rho = 1$ gm/cm^3, c = 4 J/g-C, and k = 0.006 W/cm-C [12].

RESULTS

Temperature profiles in the RPE and choroid following continuous application of 1 watt are depicted in Figure 2. A temperature gradient is rapidly established, with only modest temperature augmentation from 10–100 ms. A comparison of the early thermal transient between the RPE and deep choroid (300 μm from the RPE) is depicted in Figure 3. The temperature rise is at least biphasic with a fast early temperature rise followed by a slower rise to a plateau.

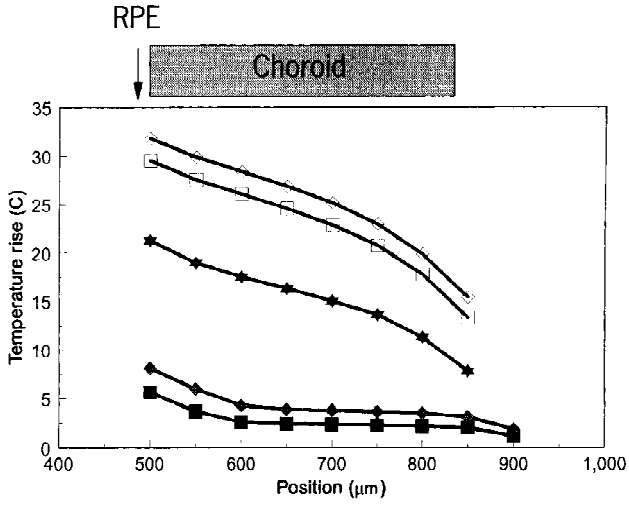

Fig. 2. Temperature profile in the ocular fundus following continuous application of 1 watt of 810 nm laser output. The RPE is arbitrarily at position = 500 μm. The temperature rise is depicted following 0.6 (filled squares), 1.0 (filled diamonds), 10 (stars), 50 (open squares), and 100 ms (open diamonds) application.

Figure 4 depicts the early thermal profile in the RPE and deep choroid in response to a train of micropulses of 2 ms duration, separated by 2 ms of quiescence. Comparison is made to the continuous mode. The temperature following the first micropulse falls to half maximum in 1.2 ms.

Since micropulsing has been invoked to minimize pain and since photocoagulative efficiency is a function of the RPE temperature, whereas pain is related to effects on sensory nerves in the deep choroid, comparisons are made between the temperature at the RPE and deep choroid (T(RPE)/T(Ch)). Figure 5 illustrates the end-pulse temperature following micropulsed off/on application. A "duty factor" of 50% is specified, i.e., the laser on and off times are equal. The magnitude of the tissue response increases with increasing micropulse length, but T(RPE)/T(Ch) achieves a maximum at ~2 ms (Fig. 6). However, the variation in T(RPE)/T(Ch) among the pulse configurations is very modest.

A comparison is made between the intra-

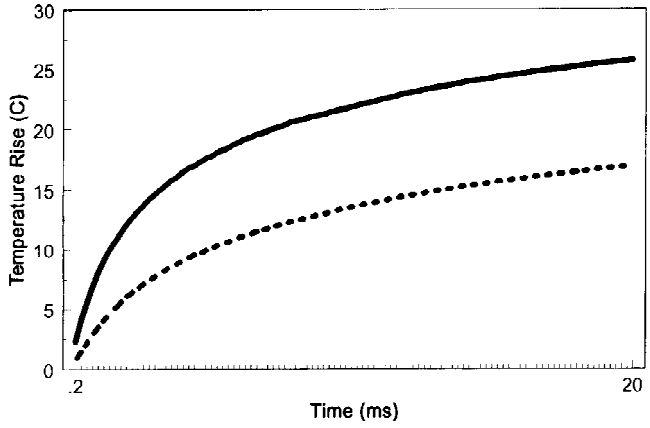

Fig. 3. Temperature rise in the RPE (solid line) and deep choroid (broken line) following 1 watt of continuous 810 nm laser application.

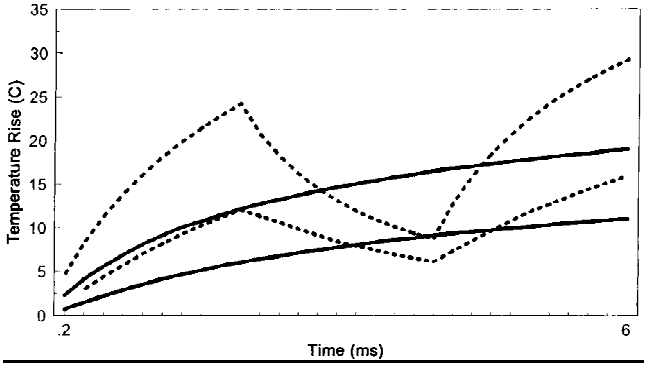

Fig. 4. Temperature rise following micropulsed (broken line) and continuous (solid line) laser application in the RPE (upper curves) and deep choroid (lower curves). Micropulsed application depicts 2 ms on/2 ms off application with a peak power of 2 W, whereas continuous mode reflects constant 1 watt application.

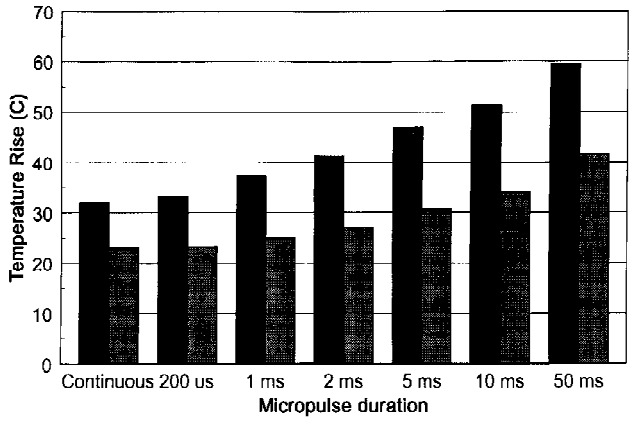

Fig. 5. The calculated temperature rise in the RPE (dark bars) and choroid (light bars) at 100 ms following continuous (1 watt) and micropulsed (2 watts peak power, duty fact = 50%) application. The total pulse length was 100 ms.

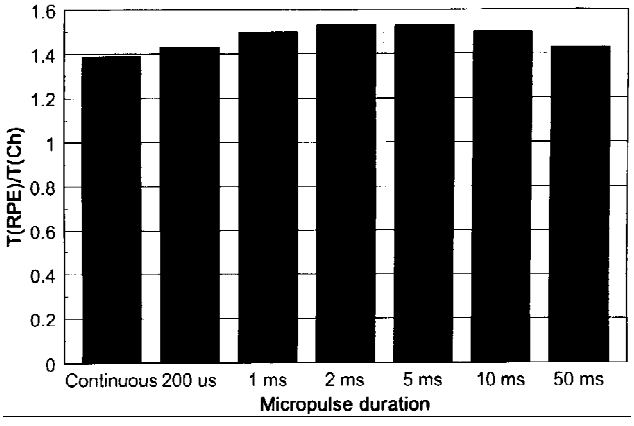

Fig. 6. The ratio of the temperature rise in the RPE to the temperature rise in the deep choroid as a function of micropulse length assuming a duty factor of 50%. Two watts peak power is applied in micropulsed application, whereas 1 watt is applied in continuous application. The total pulse length is 100 ms.

pulse T(RPE)/T(Ch) following continuous and micropulsed applications (Fig. 7). Whereas the end-pulse T(RPE)/T(Ch) is greater for 2 ms on/off application when compared with continuous mode (1.53 vs. 1.39; see Fig. 6), thermal relaxation during pulse quiescence in the micropulsed mode allows for an early *increase* in deep choroidal temperature with respect to T(RPE) (Fig. 7).

The temporal dependence of T(RPE)/T(Ch) is calculated during a short laser pulse (Fig. 8). For a 200 μs pulse, T(RPE)/T(Ch) ~3.2, decreasing to ~1.7 following 6 ms application, suggesting superior thermal localization following short pulses.

The influence of duty factor (laser "on" time divided by laser pulse duration) on thermal localization is depicted in Figure 9. For ten 200 μs pulses equally separated over 100 ms (duty factor = 2%), T(RPE)/T(Ch) = 3.2 decreasing to ~1.4 for continuous application (duty factor = 100%).

DISCUSSION

Photocoagulation is exploited for the treatment of retinal vascular diseases including proliferative diabetic retinopathy, diabetic macular edema, macular edema in the setting of venous occlusive disease, retinopathy of prematurity, exudative macular degeneration, and other diseases associated with retinal neovascularization. Early photocoagulators used non-laser sources such as sunlight [13] and xenon arc lamps; however the development of the laser stimulated investiga-

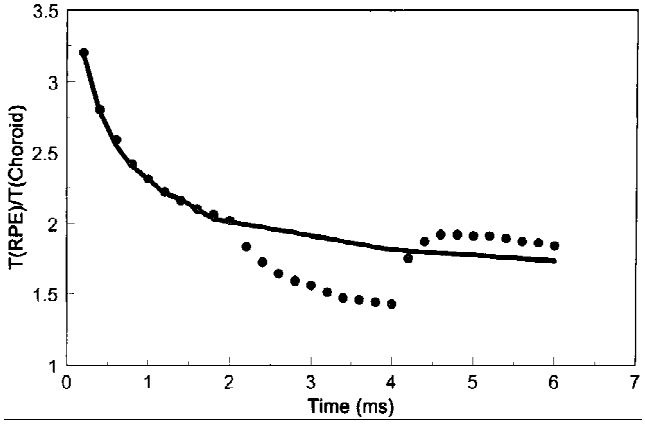

Fig. 7. The ratio of the calculated temperature rise in the RPE to the temperature rise in the choroid for continuous (1 watt, solid line), and micropulsed (2 watts peak power, 2 ms/2 ms off, dotted line) diode laser application.

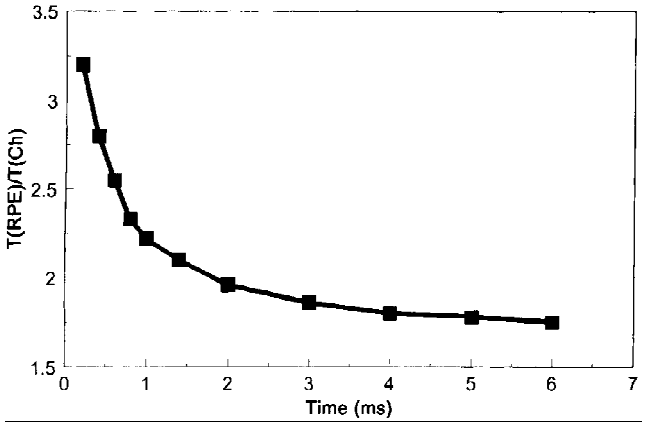

Fig. 8. The ratio of the temperature rise in the RPE to the temperature rise in the choroid during a 6 millisecond, 1 watt laser pulse. Equivalently, the data reflect the temperature ratio following single micropulse laser application where the abscissa corresponds to the duration of the micropulse.

tion yielding effective ruby [14] and argon [15] laser photocoagulators. Puliafito et al. [2] demonstrated the feasibility of using efficient and compact diode laser sources for ophthalmic photocoagulation. Diode lasers do not exploit a fundamentally distinct laser-tissue interaction, but offer economy, low maintenance, portability, and standard electrical requirements. These features are highly desirable and have stimulated considerable investigation with the intention of replacing less convenient and more costly laser sources.

Histologic studies have established that argon and diode laser sources may produce ophthalmoscopically similar lesions, but that injury resulting from diode laser application is confined to

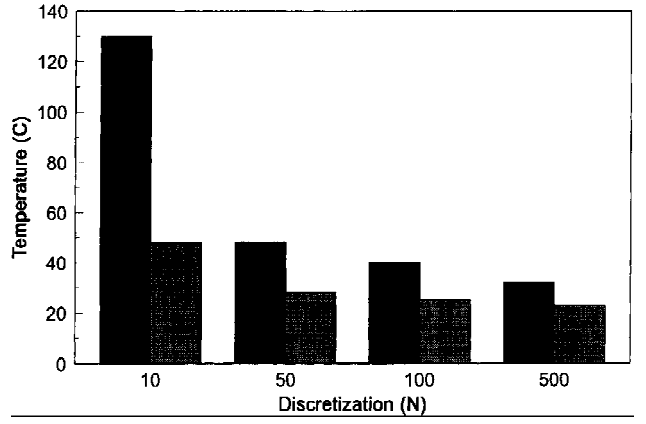

Fig. 9. The temperature rise in the RPE (dark bars) and deep choroid (light bars) following a 100 ms laser pulse with average power of 1 watt, where the laser pulse is discretized into a fixed number of equally spaced 200-μs-long micropulses. The duty factors for 10, 50, 100, and 500 micropulses are 2, 10, 20, and 100%.

the RPE and outer retina [13–16]. The relevance of this finding to the safety, efficacy, and tolerance of clinical photocoagulation is still uncertain.

Clinical reports have established that diode laser sources are potentially equi-efficacious when compared with conventional argon laser photocoagulation for macular and scatter photocoagulation [17,18]. However, patient discomfort may be greater with near-infrared diode laser photocoagulation when compared with standard visible (e.g., argon) laser techniques, presumably resulting from deeper laser penetration of infrared light through the melanin in the RPE to the sensory neurons in the deep choroid. For example, Balles et al. [3] treated 30 eyes with gallium-aluminum-arsenide diode laser radiation (805 nm) with a 200 μm spot diameter, 300–1,300 mW laser power, and with an exposure duration of 200–500 ms. They aimed for gray-white retinal lesions and reported moderate to marked pain in 43% of eyes treated with topical anesthesia. Nine patients required retrobulbar anesthesia. Alternately, Goebel et al. [19] used topical anesthesia and an ophthalmoscopically visible light gray endpoint for diode laser photocoagulation and reported no difference in pain during diode and argon laser pan-retinal photocoagulation.

However, comparison of pain between visible and near-infrared laser sources is complicated by limited information relevant to the desired clinical endpoint of retinal laser photocoagulation. Specifically, the link between an ophthalmoscop-

ically visible lesion and therapeutic efficacy is not well supported, and the potential clinical benefit of more localized injury is intriguing, yet unproven. For example, in the treatment of vasoproliferative retinopathies, stimulated RPE cells may release antiangiogenic factors independent of photoreceptor destruction [20].

The interest in diode laser micropulsing originated with the hopes of achieving thermal localization and selective tissue damage following the principle of selective photothermolysis [21]. Early work in this area confirmed that diode laser micropulses selectively damage the RPE without histologic evidence of damage to the choroid or photoreceptors [8,22]. For example, Chong and Kohen [22] delivered 100 pulses of 100 μs duration within a 200 ms envelope of 800 nm radiation to a rabbit fundus by slitlamp delivery. The retinal lesions were not visible, but electron microscopy confirmed RPE damage with sparing of the photoreceptors and choroid. In addition, Odrich et al. [23] investigated indocyanine green-enhanced diode laser sclerostomy using micropulses of 200 μs to 3 ms duration within a 1,500 ms envelope, and observed minimum surrounding tissue thermal damage for the shortest pulse durations.

Thermal localization associated with diode laser micropulsing offers the possibility of minimizing unintentional thermal tissue injury, which might be associated with photoreceptor injury, nyctalopia, and reduced visual field in scatter photocoagulation, and reduced central acuity and scotomata in macular laser applications. Further, micropulsed application may be less painful by limiting thermal diffusion to the sensory neurons in the deep choroid.

Several investigators have described their clinical studies exploiting diode laser micropulsing. Angioletti [9] studied ICG-enhanced diode laser photocoagulation of subfoveal choroidal neovascular membranes and reported less visual loss with 2 ms on/2 ms off application when compared with continuous delivery. Friberg and Venkatesh [10] compared the pain associated with diode laser photocoagulation using 300 ms continuous mode delivery with the pain associated with a sequence of 100 μs micropulses separated by 50 μs. Six of 20 patients had less pain with the micropulsed mode, whereas only one of 20 patients preferred continuous application. The authors interpreted these results to reflect thermal equilibration and cooling during pulse quiescence.

These initial studies with diode laser micropulsing cover a broad range of temporal characteristics with micropulse lengths varying from 100–3,000 μs and duty factors (laser "on" time divided by pulse duration) varying from 5–67%. The aim of this study was to investigate the influence of temporal pulse characteristics on thermal localization in order to understand previous clinical and experimental studies and to guide future investigation toward optimizing clinical outcome associated with diode laser micropulsing.

The simple model presented allows for quantitative prediction of the transient thermal tissue response to micropulsed laser application. A time-dependent temperature gradient is rapidly established (Figs. 2 and 3), and comparisons between the tissue response to continuous and micropulsed laser application can be made (Figures 4–9).

Several investigators have employed thermal modelling strategies to understand laser-tissue interactions in the ocular fundus. This model is both conceptually and calculationally straightforward, with further computational frugality achieved by confining our analysis to the axis of cylindrical symmetry through the center of a circular laser spot. The geometric and thermal assumptions reflect values in the literature to facilitate comparison with previous studies, but in part, limit the accuracy of the model [7]. In addition, several assumptions limit the flexibility of this model, but the data provide insight into the transient thermal behavior of the ocular fundus resulting from laser application, and the results presented are qualitatively similar to the more complex models of Wissler [24], Birngruber et al. [11], and Vogel and Bringruber [7]. Further, the analysis is extended to consider the thermal transients associated with laser micropulsing, which has not been previously studied.

The results presented confirm the notion that micropulsing potentially allows for thermal localization and selective injury. Further, the model allows for optimization of pulse sequence in order to exploit micropulsed application. Accordingly, the localized injury to the RPE observed by Chong and Kohen [21] is readly explicable; micropulsed application with a duty factor of 5% allows for significant thermal localization. Quantitatively, a T(RPE)/T(Ch) of 2.5 is calculated for a duty factor of 5%, compared to a value of 1.4 for continuous delivery. Equivalently, for a given RPE temperature rise, the temperature rise in the deep choroid will be nearly twice as great following continuous laser delivery.

In contrast, the operating parameters described by Friberg and Venkatesh [10] and Angi-

oletti [9] should not allow for thermal localization; appreciable thermal localization is not achieved for duty factors >20%. Alternately, nonthermal effects may contribute to the clinical endpoints of preserved vision and reduced pain. The mechanical sequelae of moderate pulse length (>1 μs) visible and near-infrared laser interactions with the ocular fundus are not well characterized; however, mechanical effects should be limited if the temperature rise is moderate such that the tissue water is not boiled.

Realization of the advantages of diode laser micropulsing is limited by available peak laser powers. For low duty factors, little total laser energy is delivered. As greater peak powers become available, shorter single pulse lengths will offer improved thermal localization (Figs. 8 and 9) possibly resulting in reduced untoward effects such as pain and unintentional tissue injury. Further, the potential benefits of selective damage to the RPE as manifested by photoreceptor preservation may be explored.

Diode lasers offer tremendous advantages over conventionally used laser sources. Compactness and portability allows for use in multiple offices, in the hospital, in the newborn nursery, and in remote, underserved areas. However, the influence of the laser pulse characteristics on the laser tissue interaction and on clinical efficacy are not well characterized. Accordingly, these modelling studies provide quantitative predictions of thermal localization achieved with diode laser micropulsing and allow for pulse-shape optimization for retinal photocoagulation applications.

REFERENCES

1. Smiddy WE, Hernandez LAT. Histopathologic results of retinal diode laser photocoagulation in rabbit eyes. Arch Ophthalmol 1992; 110:693–698.
2. Puliafito CA, Deutsch TF, Boll J, To K. Semiconductor laser endophotocoagulation of the retina. Arch Ophthalmol 1987; 105:424–427.
3. Balles MW, Puliafito CA, D'Amico DJ, Jacobson JJ, Birngruber R. Semiconductor diode laser photocoagulation in retinal vascular disease. Ophthalmol 1990; 97:1553–1561.
4. Mainster MA. Wavelength selection in macular photocoagulation: Tissue optics, thermal effects, and laser systems. Ophthalmol 1986; 93:952–958.
5. Cohen SM, Shen JH, Smiddy WE. Laser energy and dye fluorescence transmission through blood in vitro. Am J Ophthalmol 1995; 119:452–457.
6. Berger JW. Laser energy and dye fluorescence transmission through blood in vitro. Letter. Am J Ophthalmol 1995; 120:404–405.
7. Vogel A, Birngruber R. Temperature profiles in human retina and choroid during laser coagulation with different wavelengths ranging from 514–810 nm. Lasers Light Ophthalmol 1992; 5:9–16.
8. Chong LP, Kelsoe W, Donovan D, Buzawa D. Selective RPE damage by micropulsed diode laser photocoagulation. ARVO Abstracts. Inv Ophthalmol Vis Sci. 1992; 33 (Supp):722.
9. Angioletti LV. Preliminary results of ICG dye-enhanced micro-pulsed laser photocoagulation of subfoveal choroidal neovascular membranes in age-related macular degeneration. Lasers Surg Med 1995; 7 (Supp):29.
10. Friberg TR, Venkatesh S. Alteration of pulse configuration affects the pain response during diode laser photocoagulation. Lasers Surg Med 1995; 16:380–383.
11. Birngruber R, Hillenkamp F, Gabel VP. Theoretical investigations of laser thermal retinal injury. Health Physics 1985; 48:781–796.
12. Bowman HF, Cravalho EG, Woods M. Theory, measurement, and application of thermal properties of biomaterials. Ann Rev Biophysics Bioengineering 1975; 4:43–80.
13. Meyer-Schwickerath G. Koagulation der netzhaut mit sonnenlicht. Ber Deutsch Ophth Gesellsch 1949; 55:256–259.
14. Beetham WP, Aiello LM, Balodimos MC, et al. Ruby laser photocoagulation of early diabetic neovascular retinopathy. Arch Ophthalmol 1970; 83:261–272.
15. L'Esperance FA. An ophthalmic argon laser photocoagulation system: Design, construction, and laboratory investigations. Trans Am Ophthalmol Soc 1968; 66:827–904.
16. Brancato R, Pratesi R, Leoni G, Trabucchi G, Vanni U. Histopathology of diode and argon laser lesions in rabbit retina. Inv Ophthalmol Vis Sci 1989; 30:1504–1510.
17. Friberg TR. Macular photocoagulation with a diode laser. ARVO abstracts. Inv Ophthalmol Vis Sci. 1995; 36 (Supp):S440.
18. Sasoh M, Smiddy WE. Diode laser endophotocoagulation. Retina 1995; 15:388–393.
19. Goebel W, Pfeiffer N, Grehn F. Patient discomfort during laser treatment, a comparison between diode and argon laser. ARVO Abstracts. Inv Ophthalmol Vis Sci. 1994; 35 (Supp):553.
20. Glaser BM, Campochiaro PA, Davis JL, Jerdan JA. Retinal pigment epithelial cells release inhibitors of neovascularization. Ophthalmol 1987; 94:780–784.
21. Anderson R, Parrish JA. Selective photothermolysis. Science 1983; 220:524–527.
22. Chong LP, Kohen L. A retinal laser which damages only the RPE: Ultrastructural study. ARVO Abstracts. Inv Ophthalmol Vis Sci 1993; 34 (Supp):960.
23. Odrich S, Wapner F, Schubert H, Trokel S. ICG dye-enhanced micropulsed diode laser sclerostomy. ARVO abstracts. Inv Ophthalmol Vis Sci 1992; 33 (Supp):1267.
24. Wissler EH. An analysis of chorioretinal thermal response to intense light exposure. IEEE Trans Biomed Eng 1976; 23:207–215.